Clinical Investigation

Health-care-associated infections: Risk factors and epidemiology from an intensive care unit in Northern India

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ABSTRACT

Background and Aims: Health-care-associated infection is a key factor determining the clinical outcome among patients admitted in critical care areas. The objective of the study was to ascertain the epidemiology and risk factors of health-care-associated infections in Intensive Care Units (ICUs) in a tertiary care hospital. **Methods:** This prospective, observational clinical study included patients admitted in ICU over a period of one and a half years. Routine surveillance of various health-care-associated infections such as catheter-associated urinary tract infections (CAUTI), central-line-associated blood stream infections (CLABSI), and ventilator-associated pneumonias (VAP) was done by the Department of Microbiology through specific Infection Surveillance Proforma. **Results:** Out of 679 patients, 166 suffered 198 episodes of device-associated infections. The infections included CAUTI, CLABSI, and VAP. The number of urinary tract infection (UTI) episodes was found to be 73 (10.75%) among the ICU patients who had indwelling urinary catheter. In addition, for 1 year CAUTI was calculated as 9.08/1000 catheter days. The number of episodes of blood stream infection was 86 (13.50%) among ICU patients having central line catheters. Also, CLABSI was found to be 13.86/1000 central line days. A total of 39 episodes (6.15%) of VAP was found in ICU patients over 18 months and VAP present for 6.04/1000 ventilator days. **Conclusions:** The organisms most commonly associated with health-care-associated infections were *Pseudomonas aeruginosa* and *Acinetobacter* species. The risk factors identified as being significantly associated with device associated infections in our ICU were diabetes, COPD and ICU stay for ≥ 8 days ($P < 0.05$).

Key words: Epidemiology, health-care-associated infection, risk factors

INTRODUCTION

Health-care-associated infection is a key factor determining clinical outcome among patients admitted in critical care areas. Surveillance of device-associated infections has become an integral feature of infection control in all hospitals. These infections include catheter-associated urinary tract infections (CAUTI), central-line-associated blood stream infections (CLABSI), and ventilator-associated pneumonias (VAP). The Center for Disease Control and Prevention (CDC) has provided simple definitions for the diagnosis of these infections.[1] In addition, estimation of health-care-associated infection rate/1000 device days allows all hospitals to compare their rates and also recognize exclusive problem that need reappraisal. Moreover, surveillance of health-care-associated infections defines the extent and nature of problem, which is the initial step toward reducing threat of infection in vulnerable hospitalized patients.[2] Infection Control Committee, of any hospital, serves as a major tool for the surveillance of these infections. The hospitals in developed countries generate their infection-control surveillance data from time to time. This is also pertinent for empirically treating infections, especially in the intensive care

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unit (ICU) setting, where a thorough knowledge of the epidemiology, type, nature, and risk factors for infections as well as the antimicrobial resistance patterns of invading microorganism is needed.[3] It has been observed that there is scanty published data on device-associated infections available from Indian ICUs. The objective of the study was to ascertain the epidemiology and risk factors of health-care-associated infections in ICUs of a tertiary care hospital.

METHODS

This prospective study was conducted in our 750 bedded teaching hospital having two multidisciplinary ICUs consisting of five and ten beds each; from 1st May 2010 to 31st October 2011. Ours is a multidisciplinary ICU, with arrangement of each bed in a separate cubicle with nurse patient ratio of 1:3. Each bed is equipped with a single hand sanitizer fitted at foot end of the bed. The profile of patients admitted were perforation peritonitis, pneumonia, poisoning, cardiac angina, snake bite, etc., Routine surveillance of various health-care-associated infections such as CAUTI, CLABSI, and VAP was done by the Department of Microbiology through specific Infection Surveillance Performa. These forms were filled up by infection control nurse along with microbiologist and doctor in-charge of ICU.

First sample (urine, blood, and tracheal aspirate) of every patient admitted in ICU was sent for bacteriological culture to keep a baseline record to exclude infection at the time of admission into ICU, to get the true picture of infection rate. The laboratory evidence such as TLC/DLC, culture reports (repeat isolation of same bacterial strain), and other investigations like X-ray findings were correlated with the clinical findings such as temperature, pulse rate, blood pressure, auscultatory findings, and any other specific symptoms to assess infection or colonization.[1] Antibiotic susceptibility testing was carried out following Clinical Laboratory Standards Institute (CLSI) guidelines using the Kirby–Bauer method.[4] The antibiotics that were tested included amoxyclav (20/10 μg), cefotaxime (30 μg), ceftazidime (30 μg), piperacillin (100 μg), piperacillin + tazobactam (100/10 μg), imipenem (10 μg), ciprofloxacin (5 μg), norfloxacin (10 μg), gentamicin (10 μg), netilmicin (30 μg), tobramycin (10 μg), cefoxitin (30 μg), erythromycin (15 μg), vancomycin (30 μg), and linezolid (30 μg) (Hi-Media, Mumbai, India). At the end of each month the data were analyzed, and based on CDC guidelines, infection rate was calculated and presented in infection control meeting along with other issues.

The patients who were studied for diagnosis of CAUTI had an indwelling catheter *in situ* or indwelling catheter removed <7 days of onset of symptoms or symptoms appearing 48 h after insertion of catheter. A diagnosis of symptomatic UTI was made when patient had at least one of the following signs or symptoms with no other recognizable cause: Fever ≥38.8°C, urgency, frequency, dysuria, or suprapubic tenderness and patient had a positive urine culture, that is, $\geq 10^5$ microorganisms/ml of urine with no more than two species of microorganisms.[5] The diagnosis of asymptomatic bacteriuria was made when patient had an indwelling urinary catheter within 7 days before the culture and patient had a positive urine culture, that is, $\geq 10^5$ microorganisms/ml of urine with no more than two species of microorganisms and patient with no fever (38.8°C), urgency, frequency, dysuria, or suprapubic tenderness. In our study, for diagnosis of CAUTI, asymptomatic bacteriuria was included as all the patients had Foley's catheter *in situ*.

Central-line-associated blood stream infection was considered if a central line was in place for 48 h before the onset of signs and symptoms, there being no other recognized cause for positive blood culture and

- 1 positive blood culture with recognized pathogen or
- >2 blood cultures, drawn on separate occasions, positive for common skin contaminant (including *Diphtheroids*, *Bacillus*, *Propionobacterium* spp, coagulase-negative Staphylococci, viridans group Streptococci, *Micrococcus* spp).

The diagnosis of VAP was considered in patients who had a device to assist or control respiration continuously through a tracheostomy or by endotracheal intubation within the 48-h period before the onset of infection, inclusive of the weaning period. As per guidelines, VAP was diagnosed through combination of clinical, radiographical and microbiological findings as follows: Dullness to percussion on physical examination of chest and/or chest radiographic examination showing new or progressive infiltrate, consolidation, cavitations or pleural effusion and any of the following (1) New onset of purulent sputum or change in character of sputum, (2) organism isolated from blood culture, (3) positive quantitative culture from specimens like transtracheal aspirate, bronchial brushing, or lung parenchyma biopsy. In our study, quantitative transtracheal aspirates with counts of $\geq 10^6$ colony forming units/ml was used for the diagnosis of VAP.[1,6]

For all patients, data regarding the various risk factors for device associated infections were collected. These risk factors included age (>60 years), male sex, length of ICU stay (≥8 days), and various co-morbidities like diabetes type II, chronic obstructive pulmonary disease (COPD), previous hospitalization, and surgical interventions. Comparison of the aforementioned risk factors was done between the patients known to have health-care-associated infections and those without health-care-associated infections in ICU. The statistical significance of these risk factors was calculated by using the Chi square test. The factors associated with $P < 0.05$ were considered to be statistically significant. Also, the odd's ratio was calculated to ascertain the strength of association of each risk factor.

RESULTS

The total number of patients admitted in the one and a half year period in our ICU was 679, 369 male patients and 310 female patients. Age of 117 patients was more than 60 years and rest (562) were under 60 years. Among 679 patients, 334 were medical patients and 345 were postoperative patients. 28 patients had diabetes among the patients included in the study.

Out of 679 patients, 166 suffered 198 episodes of device-associated infections. Thus, the overall infection percentage was 24.44% and infection rate was 29.1%. Central-line-associated blood stream infection (13.50%) was the most common health-care-associated infection followed by UTI (10.75%) and VAP (6.15%) [Table 1]. Among the 166 patients diagnosed with device associated infections 81 died (48.7%), whereas 162 patients out of 513 (31.5%) died among the group not having device-associated infections.

All of the 679 patients had indwelling urinary catheter and total number of Foley's catheterization days was 8039. The number of UTI episodes was found to be 73 (10.75%) among the ICU patients who had indwelling urinary catheter. In addition, CAUTI was calculated as 9.08/1000 catheter days. Poly microbial infection caused by two organisms was seen in eleven cases, total of 84 uropathogens were isolated. Out of the total number of 84 urinary isolates, *Pseudomonas aeruginosa* (30) and *Enterococcus* species (13) were more commonly implicated.

A total of 637 patients had intravascular catheter (right subclavian or internal jugular) and total number of central venous line days was 6202. The episodes of blood stream infection was 86 (13.50%) among ICU patients having central line catheters. Also, CLABSI was found to be 13.86/1000 central line days. Polymicrobial infection caused by two organisms was seen in three cases; therefore, a total of 89 pathogens were isolated from blood. *Klebsiella pneumoniae* was the most commonly isolated organism from blood stream infections among ICU patients. None of the common skin contaminants including *Staphylococcus epidermidis* was established as a cause of CLABSI.

A total of 634 patients were intubated/tracheostomized and total number of ventilator days was 6455. A total of 39 (6.15%) episodes of VAP was found and for 18 months VAP was calculated as 6.04/1000 ventilator days. Polymicrobial infection caused by two organisms was seen in seven cases; therefore, a total of 46 pathogens were isolated. *Acinetobacter* species (41.03%) was the most common isolate from tracheal secretions of ICU patients.

The type and number of organisms designated as the culprits for various types of hospital acquired infection is shown in Table 2. The number of gram-negative bacilli contributing to health-care-associated infections was 183 and that of gram-positive cocci was 36. The antibiotic resistance pattern of the isolates implicated in health-care-associated infections is shown in Table 3. High degree of resistance was seen to amoxicillin-clavulanate, third generation cephalosporins, gentamicin, and netilmicin. All the Gram-negative bacilli showed maximum sensitivity to imipenem. Only 25-40% of *Pseudomonas spp*. and *Acinetobacter spp. w*ere sensitive to imipenem, while 55-90% of *E. coli* and *Klebsiella spp*. were still sensitive to carbapenem. The prevalence of MRSA was 30%. Also *Staphylococcus aureus* showed 100% sensitivity to both vancomycin and linezolid and *Enterococcus*

Table 1: Rate of health care associated infections and its associated parameters

	UTI	CLABSI	VAP
Percentage of the total health care associated infections (%)	10.75	13.50	6.15
No. of infection/1000 device days	9.08/1000 catheter days	13.86/1000 central line days	6.04/1000 ventilator days
Most common organism isolated (%)	*Pseudomonas aeruginosa* (35.7)	*Klebsiella pneumoniae* (29.2)	*Acinetobacter spp.* (41.3)

UTI – Urinary tract infection, CLABSI – Central-line-associated blood stream infections, VAP – Ventilator-associated pneumonias species showed 100% sensitivity to Linezolid, while 12.5% of the strains were resistant to vancomycin.

Comparison of various risk factors for acquiring health-care-associated infections in our ICU is shown in Table 4. The presence of diabetes and COPD as well as length of ICU stay ≥8 days was found to be significantly associated with health-care-associated infections. Age, male gender, previous hospitalization, and postoperative state were not significant associations for acquiring health-care-associated infections. Similarly by calculating the odd's ratio, the strength of association of these three risk factors (diabetes and COPD as well as length of ICU stay ≥8 days) was found to be considerable with health-care-associated infections.

Table 2: Organism isolated from various health care associated infections

Organism	Urine (%)	Blood (%)	Tracheal (%)
Acinetobacter species (51)	08 (9.5)	24 (26.9)	19 (41.3)
Pseudomonas aeruginosa (59)	30 (35.7)	13 (14.6)	16 (34.7)
Enterococcus species (25)	13 (15.4)	09 (10.1)	03 (6.5)
Klebsiella pneumonia (46)	13 (15.4)	26 (29.2)	7 (15.2)
Escherichia coli (12)	09 (10.7)	02 (2.2)	01 (2.1)
Candida species (14)	10 (11.9)	04 (4.4)	-
Staphylococcus aureus (11)	-	11 (12.3)	-
Morganella morganii (1)	01 (1.1)	-	-
Total	84	89	46

DISCUSSION

Infection surveillance analysis is an imperative prerequisite for quality care and prevention of device-associated infections. Several studies have shown that routine surveillance of these infections can reduce the incidence by as much as 30%.[7] However, in developing countries, due to lack of formal surveillance the rate of health-care-associated infections is high and compliance with hand hygiene is low.

In India, the rate of device-associated infections shows variations and has great implication. Habibi *et al.* in their study from AIIMS, Delhi, India, found the incidence rates of health-care-associated infections to be 11.3/1000 urinary catheter days, 3.4/1000 central venous pressure line days and 31.4/1000 ventilator days.[8] In the ICU's of seven hospital members of the international infection control consortium (INICC) of seven Indian cities the

Table 3: Antibiotic resistance percentage of various pathogens causing health-care associated infections

Antibiotic	*Acinetobacter* species (51) (%)	*Pseudomonas aeruginosa* (59) (%)	*Klebsiella pneumoniae* (46) (%)	*Escherichia coli* (12) (%)	*Enterococcus* species (25) (%)	*Staphylococcus aureus* (11) (%)
Amoxicillin+clavulanic acid	-	-	100	100	100	-
Cefotaxime	90.3	83.3	96.3	84.6	-	-
Ceftazidime	95.8	94.4	94.1	100	-	-
Piperacillin	64.3	92.9	100	83.3	-	-
Piperacillin+Tazobactam	50	77.8	71.4	62.5	-	-
Imipenem	57	76.8	46.7	11.8	-	-
Ciprofloxacin	69.7	61.1	89.5	91.7	80	72.7
Norfloxacin	-	-	100	100	100	-
Gentamicin	88.9	84.6	91.7	81.8	90	67
Netilmicin	85.7	93.3	71.4	66.7	63.6	66.7
Tobramycin	90	95.6	83.3	-	-	-
Cefoxitin	-	-	-	-	-	30
Erythromycin	-	-	-	-	88.9	60
Vancomycin	-	-	-	-	12.5	0
Linezolid	-	-	-	-	0	0

Table 4: Risk factors for the development of health-care-associated infections

Risk factor	Patients with health-care-associated infections; *n*=166 (%)	Patients without health-care-associated infections; *n*=513 (%)	*P* value	Odd's ratio
Age≥60 years	32 (19.27)	85 (16.56)	0.422	1.20
Male sex	97 (58.43)	272 (53.02)	0.224	1.24
Diabetes mellitus type II	12 (7.22)	16 (3.11)	0.0215	2.42
Previous surgery	85 (51.20)	260 (50.68)	0.906	1.02
ICU stay≥8 days	153 (92.16)	248 (48.34)	<0.001	12.57
Previous hospitalization	13 (7.83)	26 (5.06)	0.185	1.59
COPD	81 (48.7)	162 (31.57)	<0.001	2.06

COPD – Chronic obstructive pulmonary disease, ICU – Intensive care unit overall infection rates were 1.41/1000 catheter days for CAUTI, 7.92/1000 catheter days for CLABSI and 10.46/1000 ventilator days for VAP.[9] Considering these values, the rate of VAP was relatively less where as CLABSI was significantly higher in our hospital ICU's. Rates were comparable with that of 55 ICUs in developing countries (CAUTI-8.9/1000 catheter days, CLABSI- 12.8/1000 catheter days and VAP - 24/1000 ventilator days).[10] This reflects the importance of generating and evaluating own hospital data for development of proper infection control programme.

The occurrence of CLABSI depends upon the site, type of catheter, frequency of catheter manipulation, and patient's primary illness. There is evidence that the use of central line through the subclavian access (in contrast to internal jugular or femoral access) reduces infection rates.[11] In our institute various reasons for increased incidence of CLABSI include multidisciplinary ICU, less stringent infection control practices and high cost of alcoholic hand disinfectant that is not available at the bed side of all patients. Berenholtz *et al.* found a significant decline in CLABSI after following five points intervention module in their surgical ICU. The intervention module included education of staff, creating a catheter insertion cart, asking providers each day whether catheters could be removed, implementing a checklist to ensure the adherence to evidence-based guidelines for preventing CLABSI and empowering nurses to stop the catheter insertion procedure if a violation of the guidelines was observed.[12]

The relative lower incidence of CAUTI and VAP could be because of vigilant nursing care. The nurses in our ICUs take care of catheter in the form of cleaning of catheter entry site and several inches of the tubing daily and after bowel movement, emptying of urobags after fixed period of time, keeping the urobags always below the bladder, etc.[13] For the prevention of VAP, the patients are kept in the semirecumbent position, draining of condensate is performed from ventilator circuits after a particular time period (after 4-6 h or earlier if need); continuous subglottic suctioning is performed, adequate pressure is maintained in endotracheal-tube cuff (palpation method), and strict adherence to all the elements of ventilator bundle protocol.[14]

In comparison to gram-positive bacteria, gram-negative bacteria were more commonly isolated from cases of health-care-associated infections. *P. aeruginosa* and *Acinetobacter* species that are widely known to be the most common cause of health-care-associated infections were also found to be the most culpable organisms in our ICUs. Similar picture has been observed by other investigators.[8,15-17] The study of Agarwal *et al.* in another institute, from our geographical region, also found majority of infections with gram-negative bacilli in respiratory ICU. Moreover, *Acinetobacter* species followed by *P. aeruginosa* were found to be the most common cause of pneumonia.[18]

The mortality rate was higher in the group of patients having device-associated infections as compared to those who did not have them. As predicted, high drug resistance rate and limited drug options for these patients were seen. Many of the isolates were resistant to all the drugs tested. A very high resistance was observed to third generation cephalosporins (ceftazidime and cefotaxime). The organisms even showed high resistance to beta lactam and beta lactamase inhibitor combination (piperacillin + tazobactam) and carbapenems (imipenem) thus limiting their importance as single drug empirical therapy in ICUs. In our ICUs, methicillin resistant *staphylococcus aureus* (MRSA) was found in 30% although no resistance to vancomycin and linezolid was seen in *S. aureus* isolates. Scenario of high resistance was noticed with aminoglycosides and quinolones in both Gram-positive and Gram-negative organisms. For Gram-positive cocci, although a high resistance to other commonly used drugs was seen, yet vancomycin and linezolid were found to be of utmost importance in case of multidrug resistance. But, the disappointing fact was the isolation of vancomycin-resistant enterococci (VRE) from the samples. This increases the morbidity and escalates the cost of treatment; thus the infection control team should strictly reinforce use of proper barrier precautions, the importance of aseptic techniques and hand washing. We did not find glycopeptides resistance in *Staphylococcus* isolates. Kamat *et al.* have reported 11.8% vancomycin resistance in their nosocomial *Staphylococcus* isolates from Goa.[15]

In our study, age and gender are not significantly associated with development of infections in ICU; similar outcome has been shown by Meric *et al.* and Agarwal *et al.*[18,19] The risk factors which were considerably linked with health-care-associated infections include length of ICU stay. Various authors have cited this as being an important reason for development of infection.[8,18-20] The longer the patients stays in ICU more are the chances of getting colonized with multidrug-resistant bacteria and longer will be the time period of insertion of devices. Moreover, diabetes and COPD were significant associations in patients with infections. A related study from India has shown these two factors not to be related with development of health-care-associated infections.[8] This may be because patients with diabetes and COPD come at terminal stage when they are highly immunosuppressed making them highly susceptible to health-care-associated infections and multidrug-resistant bacteria present in the ICU environment. Previous hospitalization and postoperative state, though not appreciably associated with health-care-associated infections in our ICU, were important risk factors in other hospital settings.[20]

There are several pit falls of our study. There may be generalization of the factors since all the patients admitted in ICU for 18 months were included in the study. Severity of illness (SOFA or APACHE) scores as important risk factors were not assessed. Data regarding various catheter insertion sited like subclavian vein, internal jugular vein and femoral veincould have been analyzed to check for any relationship between them and CLABSI.

CONCLUSIONS

This study documents a high prevalence rate of CLABSI in our ICUs and high frequency of multidrug-resistant *P. aeruginosa* and *Acinetobacter species*. The following risk factors were identified as being significantly associated with device-associated infections in our ICU; diabetes, COPD, and ICU stay for ≥8 days ($P < 0.05$). Interventions to control spread of these resistant bacteria include optimizing antibiotic selection and dosing, strict adherence to infection control practices, and rational use of antimicrobial combinations.

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